

**UNITED STATES DISTRICT COURT  
DISTRICT OF NEW JERSEY**

**IN RE: JOHNSON & JOHNSON  
TALCUM POWDER PRODUCTS  
MARKETING, SALES  
PRACTICES, AND PRODUCTS  
LIABILITY LITIGATION**

**MDL No. 16-2738 (MAS) (RLS)**

***THIS DOCUMENT RELATES TO  
ALL CASES***

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**THE PLAINTIFFS' STEERING COMMITTEE'S RESPONSE TO THE  
COURT'S APRIL 30, 2024 MEMORANDUM AND ORDER REGARDING  
JUDGE WOLFSON'S *DAUBERT* OPINION ON GENERAL CAUSATION**

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## **TABLE OF CONTENTS**

INTRODUCTION & BACKGROUND .....	1
DISCUSSION .....	4
I. CHIEF JUDGE WOLFSON’S PREVIOUS OPINION FULLY ADHERES TO RULE 702, EVEN AS CLARIFIED BY THE 2023 AMENDMENTS ...	4
II. THE “NEW SCIENCE” PUBLISHED SINCE 2020 REGARDING THE GENITAL USE OF TALC AND OVARIAN CANCER DOES NOT CONTRADICT CHIEF JUDGE WOLFSON’S 2020 GENERAL CAUSATION FINDINGS AND <i>DAUBERT</i> DECISION. ....	12
A. Strength of Association: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That Genital Talc Use Is Associated With An Increased Risk of Ovarian Cancer .....	17
1. O’Brien (2020).....	19
2. O’Brien (2024).....	24
3. Woolen (2022) .....	26
B. Consistency of Association: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence of “Consistency” Between Studies Of Genital Talc Use And Ovarian Cancer .....	27
C. Biologic Plausibility: Post-2020 Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence Supporting Plaintiffs’ Claim That It Is Biologically Plausible That Talc Causes Ovarian Cancer ..	30
D. Dose Response: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence Supporting A Dose Response Between Genital Talc Use And Ovarian Cancer .....	32
E. Actions By Authoritative National And International Scientific Bodies After Judge Wolfson’s 2020 <i>Daubert</i> Opinion Further Support A Causal Effect.....	34
1. Health Canada .....	34
2. The International Agency for Research on Cancer (IARC) .....	35
3. The Environmental Protection Agency.....	36
4. National Institutes of Health .....	37

CONCLUSION .....	37
------------------	----

## **TABLE OF AUTHORITIES**

### **Cases**

<i>Carl v. Johnson &amp; Johnson</i> , 464 N.J. Super. 446 (App. Div. 2020) .....	18
<i>Carl v. Johnson &amp; Johnson</i> , Nos. ATL-L-6540-14, 2016 N.J. Super. Unpub. LEXIS 2102, 2016 WL 4580145 (N.J. Super. Ct. Sept 2, 2016) .....	18
<i>In re: Johnson &amp; Johnson Talcum Powder Prods, Mktg., Sales Practices &amp; Prods. Litig.</i> , 599 F. Supp. 116 (D.N.J 2020) .....	passim
<i>Milward v. Acuity Specialty Prods. Grp., Inc.</i> , 639 F.3d 11 (1st Cir. 2011) .....	30

### **Rules**

Fed. R. Evid. 702 .....	2
-------------------------	---

### **Treatises**

Michael D. Green, et al., Reference Manual on Scientific Evidence - <i>Reference Guide on Epidemiology</i> 549, 600 (Fed. Jud. Ctr., 3d Ed. 2011) .....	7
-------------------------------------------------------------------------------------------------------------------------------------------------------------	---

### **Regulations**

88 Fed. Reg. 47782 (July 25, 2023) (to be codified at 40 C.F.R. pt. 704) .....	36
89 Fed. Reg. 21970 (May 28, 2024) (to be codified at 40 C.F.R. pt. 751) .....	15, 36

## **INTRODUCTION & BACKGROUND**

On April 30, 2024, this Court denied the Plaintiffs' Steering Committee's (PSC) Motion For Reconsideration Of The Court's March 27, 2024 Text Order Allowing A Full Refiling Of Daubert Motions.<sup>1</sup> To the extent either party sought to address anew the issue of "general causation" raised by Chief Judge Wolfson's 2020 *Daubert* ruling,<sup>2</sup> the Court gave the parties guidelines for refiling *Daubert* Motions. Specifically, the Court directed that the parties "should identify either (1) that Chief Judge Wolfson's previous Opinion demonstrably fails to adhere to Rule 702 as clarified by the 2023 amendments; or (2) new science is shown to directly contradict or challenge Chief Judge Wolfson's previous findings."<sup>3</sup>

The parties have now completed expert discovery on the general causation issues, including any methodologic issues incorporating "new science" which have been published since April 2020. For the reasons set forth in this memorandum, the PSC responds to this Court's questions as follows: (1) Chief Judge Wolfson's *Daubert* Opinion adheres to Rule 702, even as clarified by the 2023 amendment; and (2) the science and literature published since 2020 does not contradict Chief

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<sup>1</sup> Memorandum Order, April 30, 2024 (Doc. 32122) ("April 30 Order") at 6.

<sup>2</sup> *In re: Johnson & Johnson Talcum Powder Prods, Mktg., Sales Practices & Prods. Litig.*, 599 F. Supp. 116 (D.N.J 2020) ("*Daubert* Opinion").

<sup>3</sup> April 30 Order at 6.

Judge Wolfson’s previous findings but demonstrate that the *Daubert* Opinion regarding general causation was correct.

As discussed below, in 2019, Chief Judge Wolfson conducted an eight-day hearing and used the “preponderance of the evidence” standard subsequently clarified in amended Rule 702.<sup>4</sup> Since both the causation methodology and application of that methodology to the talc science by both sides is, as Defendants’ experts agree, exactly the same as it was when Judge Wolfson considered it in 2020, there is no basis for a Rule 702 challenge. Further, the so called “new science” relied on by Defendants to justify reconsideration does not come close to “contradict[ing] or challeng[ing] Judge Wolfson’s previous findings.” In fact, even the “preeminent scientists” at the National Institute of Health (NIH) that Defendants previously proffered to justify unwinding Chief Judge Wolfson’s opinion<sup>5</sup> asserted within the last two months that there *is* a “consistent association

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<sup>4</sup> Fed. R. Evid. 702. (“A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if the proponent ***demonstrates to the court that it is more likely than not that...***” (emphasis added)).

<sup>5</sup> See, e.g., Defendants’ Opposition to Plaintiffs Steering Committees Motion for Reconsideration of the Courts March 27, 2024 Text Order Allowing A Full Refiling Of Daubert Motions, (filed April 22, 2024) (ECF No. 32026) at 16. (“Additional scientific evidence published by preeminent epidemiologists, including from the National Cancer Institute and the National Institute of Environmental Health Sciences, has further undermined the reliability of plaintiffs’ evidence of general causation.”) (referring to, among others, NIH scientists Katie O’Brien, Ph.D. and Nicholas Wentzensen, M.D. Ph.D.).

between talc use and ovarian cancer.”<sup>6</sup> Also, this month, those very same scientists who sat on a panel of the World Health Organization’s International Agency for Research on Cancer (IARC) published their findings that talcum powder *without* asbestos is a “probable” Group 2A ovarian carcinogen and reaffirmed that talcum powder *with* asbestos is a Group 1 or known ovarian carcinogen.<sup>7</sup> IARC’s conclusion follows the determination of Health Canada, which in 2021, after conducting a full Bradford Hill causation analysis, concluded that there is a causal connection between genital exposure to talcum powder and ovarian cancer.<sup>8</sup> Significantly, the Health Canada determination was made in the face of Defendants’ ongoing lobbying efforts and their experts having provided ongoing input.

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<sup>6</sup> NIH/NIEHS Environmental Factor, *Genital Talc Use May Be Linked To Increase Risk Of Ovarian Cancer—New Study By NIEHS Scientists Provides Compelling Evidence That Genital Talc Use Is Associated With And Increased Risk Of Ovarian Cancer* (June 2024), attached as **Exhibit 1**.

<sup>7</sup> Stayner et al., *Carcinogenicity of Talc and Acrylonitrile*, *The Lancet* (July 5, 2024), attached as **Exhibit 2**; see also *IARC Monographs Evaluate The Carcinogenicity of Talc and Acrylonitrile: Questions and Answers* (July 5, 2024) at 3-5, attached as **Exhibit 3**.

<sup>8</sup> See Health Canada, *Screening Assessment Talc* (April 2021) (“Health Canada Screening Assessment”), attached as **Exhibit 4**.

## **DISCUSSION**

### **I. CHIEF JUDGE WOLFSON’S PREVIOUS OPINION FULLY ADHERES TO RULE 702, EVEN AS CLARIFIED BY THE 2023 AMENDMENTS**

In the Court’s April 30, 2024 ruling allowing challenges to Judge Wolfson’s 2020 *Daubert* decision, the Court focused any new challenge on whether Judge Wolfson’s prior *Daubert* Opinion did not comply with Rule 702 (as amended). The Court noted that the challenging party carries the burden of demonstrating that Judge Wolfson’s ruling “demonstrably” departed from Rule 702 requirements.<sup>9</sup>

Judge Wolfson properly followed the requirements of Rule 702, and her opinion thoroughly and comprehensively meets any requirement that amended Rule 702 may have clarified. Defendants cannot demonstrate that Judge Wolfson’s opinion was a departure from Rule 702 or that it should not be given full deference because the amendments to Rule 702 do not undermine the analysis or rationale. Indeed, to the extent the Rule 702 amendments clarified there is a preponderance of evidence standard, Judge Wolfson clearly applied the appropriate preponderance of evidence standard.

As a preliminary matter, Judge Wolfson’s exhaustive opinion examined in detail the full methodologic and scientific challenges raised by both sides as to all causation experts. In addition to hundreds of pages of briefing, the Court held an

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<sup>9</sup> April 30 Order at 6.



eight-day evidentiary hearing where experts for both sides appeared and were examined. During the hearing, Judge Wolfson was an active participant, often posing specific questions which were obviously designed to “test” each witness’s understanding of the evidence. Judge Wolfson probed the parties’ application of each Bradford Hill factor and the applicability of each factor to the scientific evidence. Then, and only then, did Judge Wolfson specifically ***apply the preponderance of evidence standard***. Indeed, Judge Wolfson referenced that standard explicitly in the Opinion:

In conclusion, what remains clear from the general causation evidence relied on by the experts on both sides in this matter, is that there is scientific evidence supporting each side’s opinion.... Ultimately, the question of whose experts are correct is a question for the jury; it would be erroneous for this Court to make those factual findings on a *Daubert* motion. *See Mitchell*, 365 F.3d at 244 (“*Daubert* does not require that a party who proffers expert testimony carry the burden of proving to the judge that the expert’s assessment of the situation is correct” (quoting *Ruiz–Troche*, 161 F.3d at 85)); *In re Processed Egg Prods. Antitrust Litig.*, 81 F. Supp. 3d 412, 416 (E.D. Pa. 2015) (“Proponents of expert testimony do not ‘have to prove their case twice—they do not have to demonstrate to the judge by a preponderance of the evidence that the assessments of their experts are correct, ***they only have to demonstrate by a preponderance of evidence that their opinions are reliable.***” (Citation omitted)).<sup>10</sup>

The record is indisputable that Judge Wolfson performed a thorough and proper “preponderance of evidence” review of the available scientific expert evidence. That said, it is helpful to note that Judge Wolfson applied the same

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<sup>10</sup> *Daubert* Opinion, 509 F. Supp. 3d at 187; *see also id.* at 147-48.

general causation methodology that was being used *independently* and contemporaneously by Health Canada (the Canadian government's regulatory agency comparable to the FDA) in evaluating the evidence presented here. Health Canada, in a non-judicial setting, employed the same methodology that Judge Wolfson used to evaluate expert opinions on general causation.<sup>11</sup>

Importantly, Health Canada did an independent "Evaluation of Causation" using not only the *exact same* framework discussed by Judge Wolfson, but also considered the reports of the *exact same* experts and applied the *exact same evidentiary foundation and framework*. In the Final Screening Assessment, Health Canada stated:

*Evaluation of Causation*

The Hill considerations are a set of factors (i.e., strength, consistency, specificity, biological gradient, biological plausibility, coherence, experiment and analogy) that can form a framework for evaluating evidence in humans to help determine whether observed associations may be causal (Hill 1965; Coglianò et al 2004; U.S. EPA 2005; Fedak et al. 2015).

Established several decades ago, the Hill considerations continue to be employed today, with some modified interpretations; there is general consensus that some factors hold more weight than others. Strength, consistency and biologic gradient are most frequently considered. Conversely, experiment, analogy and specificity are often considered to be less significant, or to hold less weight, in the decision-making framework (Grimes and Schultz 2002; Carson 2018; Kane 2018;

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<sup>11</sup> Health Canada Screening Assessment, Ex. 4, at 16-36.

Moorman 2018; Singh 2018; Smith 2018; Wolf 2018; Ballman 2019; Diette 2019; Merlo 2019).<sup>12</sup>

Additionally, Judge Wolfson was presented with and considered the very same scientific arguments in advance of her 2020 *Daubert* Opinion that Defendants asserted to Health Canada. Based on the totality of the evidence, Judge Wolfson concluded that the parties demonstrated by a preponderance of evidence that the expert opinions should be submitted to the jury. And Health Canada similarly determined that there was sufficient evidence to conclude that talcum powder could cause ovarian cancer:

With regards to perineal exposure, analyses of the available human studies in the peer-reviewed literature indicate a consistent and statistically significant positive association between perineal exposure to talc and ovarian cancer. The available data are indicative of a causal effect.<sup>13</sup>

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<sup>12</sup> Health Canada Screening Assessment, Ex. 4, at 29. In her opinion, Judge Wolfson noted the very same standard:

Plaintiffs' experts formed their general causation opinions using the Bradford Hill criteria, "which are nine factors widely used in the scientific community to assess general causation." *Gannon*, 292 F. App'x at 172-73. Those nine factors are (1) temporal relationship; (2) strength of association; (3) dose-response relationship; (4) replication; (5) biological plausibility; (6) consideration of alternative explanations; (7) cessation of exposure; (8) specificity of the association; and (9) consistency with other knowledge. Michael D. Green, et al., *Reference Manual on Scientific Evidence - Reference Guide on Epidemiology* 549, 600 (Fed. Jud. Ctr., 3d Ed. 2011).

*Daubert* Opinion, 509 F. Supp. at 160.

<sup>13</sup> Health Canada Screening Assessment, Ex. 4, at iii.

Notably, both Judge Wolfson and Health Canada used the same Bradford Hill framework and considered the same arguments on the same scientific evidence and experts. To give but a few specific examples:

- Judge Wolfson considered J&J's experts' (Diette & Merlo) claim that the Talc cohort studies are always superior to Talc case-control studies, and Plaintiffs' experts' contrary opinion (McTiernan & Siemiatycki), in exactly the same fashion that Health Canada did.<sup>14</sup>
- Judge Wolfson considered J&J's experts' (Diette & Merlo) claim that a "small" increased risk of 1.3 seen in the Talc studies must be explained by "bias and confounding" and Plaintiffs' experts (McTiernan & Siemiatycki) contrary opinion that a "modest" association can be causal, just as Heath Canada had.<sup>15</sup>
- Judge Wolfson considered whether a strict adherence to "statistical significance," *i.e.* "statistical testing" was required, as J&J's experts (Diette & Merlo) contended and Plaintiffs' experts' argument that it is not - just as Heath Canada did.<sup>16</sup>
- Judge Wolfson considered the argument that there was no biologically plausible mechanism to support a causal inference that Talc causes ovarian cancer offered by J&J's expert (Diette) and Plaintiffs' experts' (Siemiatycki, Singh and McTiernan) contrary view that there was such evidence.<sup>17</sup>

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<sup>14</sup> Compare Heath Canada Screening Assessment, Ex. 4, at 31 *with* Daubert Opinion, 509 F.Supp.3d at 161.

<sup>15</sup> Compare Heath Canada Screening Assessment, Ex. 4, at 30 *with* Daubert Opinion, 509 F.Supp.3d at 165, 191.

<sup>16</sup> Compare Heath Canada Screening Assessment, Ex. 4, at 31 *with* Daubert Opinion, 509 F.Supp.3d at 158-159.

<sup>17</sup> Compare Heath Canada Screening Assessment, Ex. 4, at 31 *with* Daubert Opinion, 509 F.Supp.3d at 172-176.

- Judge Wolfson considered J&J's contention that only bias and confounding could explain the increased risk of ovarian cancer seen in most of the epidemiologic studies as proposed by J&J and its experts (Diette and Merlo), and also considered the counter argument from plaintiffs' experts (Siemiatycki, Singh & McTiernan), that these factors cannot account for the consistent associations produced epidemiologic across studies just as Heath Canada did.<sup>18</sup>

In short, this peer-reviewed causation assessment by a regulatory agency provides external validation of Judge Wolfson's legal approach to the reliability of the exact same evidence. In the case of Health Canada, it applied that framework and methodology to reach the conclusion that the weight of the evidence,<sup>19</sup> *i.e.*, a preponderance of reliable scientific evidence that talcum powder, can cause epithelial ovarian cancer and banned it from sale in that country.<sup>20</sup> Using that same approach and considering essentially the same evidence, Judge Wolfson ruled that the reliability of Plaintiffs' experts' opinions was demonstrated by a preponderance of the evidence and left the causation question to the jury.

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<sup>18</sup> *Compare* Health Canada Screening Assessment, Ex. 4, at 35 *with* Daubert Opinion, 509 F.Supp.3d at 181.

<sup>19</sup> Heath Canada Screening Assessment, Ex. 4, at 35 ("ovarian cancer-weight of evidence")

<sup>20</sup> "Overall, there is a high degree of consistency in the epidemiological studies across several decades conducted in different parts of the world. Although there are uncertainties related to bias, there is confidence in the robustness of the available database for use in characterizing ovarian cancer risk attributed to talc exposure. ***Furthermore, the available data are indicative of a causal relationship.***" Health Canada Screening Assessment, Ex. 4, at 36.

Moreover, Defendants' experts have not articulated any methodological change between the current evidence presented by both sides and what was provided to the Court in advance of the 2020 *Daubert* Opinion. In 2024, Defendants' experts have admitted that both they and Plaintiffs' experts used the identical methodologies used in 2020. For example, Defendants' expert, Dr. Diette, testified that the methodologies for all experts today are the same as what was considered in 2019:

Q. Is it fair to say that the methodology that you employed -- for purposes of giving all the opinions you're going to be sharing with us today -- are the same methodologies that you used back in 2019?

A. Yeah. It's all fundamentally the same, same methodology.

Q. So the methods that you employed with regard to assessing causality in 2019 remain the same methodology that you used in 2024?

A. Correct.

Q. **All right. Now is the methodology that you employed for purposes of assessing causality for your report in 2024, the same methodology that you used when you testified before Judge Wolfson in the Daubert proceeding back in July of 2019?**

A. **Yes, yeah. The fundamentals are all the same.**

Q. All right. At the time that you addressed Judge Wolfson, Chief Judge Wolfson --who was overseeing the multidistrict litigation -- you had reviewed the literature?

A. Yeah, the available literature to date.

Q. All right. You had assessed the Bradford Hill factors in determining causality?

A. I had.

Q. All right. You considered the influence on study findings of bias, confounding and other sorts of errors, correct?

A. Yeah, in addition to the Bradford Hill considerations.

Q. All right. And you also looked at the different study designs, their strengths and their weaknesses, correct?

A. Correct.

Q. All right. You've also had an opportunity to review the expert reports of some of the plaintiff's experts who are testifying, correct?

A. That is correct.

Q. **All right. And based upon your review of the updated reports of the plaintiff's experts -- and comparing them to their reports that they also prepared back in 2018 -- you understand that those experts also employed the same methodology?**

A. **It seemed -- it seemed so to me. I didn't see any, you know, fundamental differences in the methodology.**<sup>21</sup>

One of J&J's other general causation expert, Dr. Merlo, said the same:

Q. Putting aside plaintiffs' experts' interpretations of new studies after 2019, can you think of any additional methodologic principle or method that plaintiffs' experts failed to apply when

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<sup>21</sup> Diette Dep. at 31:11-34:13 (June 19, 2024) (emphasis added), attached as **Exhibit 5**.

assessing the literature that is not captured in your criticisms from 2019?

A. I think it's contained in my 2024 report.

Q. *Right. And in terms of methodology, there's no difference?*

A. *That's my opinion. Yes.*<sup>22</sup>

With that background, neither the PSC nor Defendants can credibly say that Judge Wolfson failed to conduct a thorough review of the evidence considering basic scientific principles. Nor can it be said that Judge Wolfson failed to apply a preponderance of evidence standard to conclude that the general causation experts used a reliable methodology. The parallel Heath Canada review and causation assessment supports the finding that the Plaintiffs' experts' opinions reliably used a preponderance of evidence standard. In addition, the parties' joint acknowledgment that no new methodology has been used by the experts supports leaving Judge Wolfson's findings undisturbed.

## **II. THE "NEW SCIENCE" PUBLISHED SINCE 2020 REGARDING THE GENITAL USE OF TALC AND OVARIAN CANCER DOES NOT CONTRADICT CHIEF JUDGE WOLFSON'S 2020 GENERAL CAUSATION FINDINGS AND *DAUBERT* DECISION.**

In response to this Court's second basis to challenge Judge Wolfson's 2020 *Daubert* decision, there is no "new science [] to directly contradict or challenge

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<sup>22</sup> Merlo Dep. at 34:6-35:2 (June 14, 2024) (emphasis added), attached as **Exhibit 6**.



Judge Wolfson’s previous findings.” Indeed, since 2020, scientific studies published by independent scientists as well as national and international scientific bodies, have concluded that talc, both with and without asbestos, *can cause* ovarian cancer.

The basis for Plaintiffs’ expert’s opinions remains the same as it was in 2018 — that talcum powder is capable of causing epithelial ovarian cancer because:

- There is a consistent association, across decades of epidemiologic studies of different designs and with different researchers that have demonstrated genital talc use is associated with a risk of epithelial ovarian cancer.
- The increased risk of epithelial ovarian cancer seen in these studies is between 30-60%.
- There is a dose response because risk increases with both frequency and duration of genital talc use.
- It is biologically plausible that genital talcum powder causes ovarian cancer based upon evidence that:
  - Talcum powder can migrate from the perineal area, through the open female genital tract, and reach the fallopian tubes and ovaries where it can create an inflammatory response.
  - Talcum powder generally, and Johnsons Baby Powder and Shower to Shower specifically, contain known carcinogens, including asbestos, fibrous talc, and heavy metals.

Judge Wolfson was correct when deciding *Daubert* in 2020. That said, the scientific and regulatory evidence has continued to develop since 2020 and the

case for causal association is both stronger and confirmatory. With respect to scientific studies, the vast majority of post-2020 evidence comes from prospective cohort studies—the very types of studies that Defendants’ experts previously argued to Judge Wolfson were the most appropriate studies to evaluate the association between genital talc use and ovarian cancer. The post-2020 cohort studies are summarized as follows:

- **Strength of Association:** The new cohort study data, primarily from independent scientists at National Institutes of Health (NIH), shows a statistically significant positive association between genital talc use and ovarian cancer in women with an open genital tract<sup>23</sup> and frequent users.<sup>24</sup> These post-2020 cohort study findings provide further support to the 1.2 to 1.4 (20-40%) relative risk range seen in other studies that Judge Wolfson considered in her 2020 *Daubert* Opinion.<sup>25</sup>
- **Consistency of Association:** The NIH researchers have noted that their post-2020 epidemiologic studies on the whole support the consistency factor for causation since, according to the researchers, their most recent studies were “consistent with previous studies, pooled analyses or metaanalysis of case control studies that have produced odds ratios of 1.2 to 1.4”<sup>26</sup> as well as a “positive association” in 2020 pooled analysis the NIH scientists conducted

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<sup>23</sup> Katie M. O’Brien, et al., *Association of Powder Use in the Genital Area with Risk of Ovarian Cancer*, 323 JAMA 49 (2020), attached as **Exhibit 7**.

<sup>24</sup> Katie M. O’Brien, et al., *Intimate Care Products and Incidence of Hormone-Related Cancers: A Quantitative Bias Analysis*, J. Clin. Oncology (2024) (“The association between genital talc use and ovarian cancer was higher for frequent, 1.81 [], and long-term users, 2.01 [], compared with never users.”), attached as **Exhibit 8**.

<sup>25</sup> *Daubert* Opinion at 162-167.

<sup>26</sup> O’Brien (2024), Ex. 8 at 13 (citing Taher (2019), Penninkilampi (2018), Terry (2013), Berge (2018) and Davis (2021)).

“of prospective cohort studies.”<sup>27</sup> As the NIH has itself noted, there is now a “persistent positive association between genital talc use and ovarian cancer, with the strongest associations observed for frequent and long term users.”<sup>28</sup> Previously, Judge Wolfson noted that the cohort studies were positive but not statistically significant, a fact that has changed since 2020. This is further support for Judge Wolfson’s position that there is reliable evidence on this specific Bradford Hill factor.<sup>29</sup>

- **Biologic Plausibility:** Similarly, the case for biologic plausibility that was discussed by Judge Wolfson in 2020 has gotten stronger and has become more generally accepted and established in scientific literature. The observations of the NIH scientists are illustrative, noting that talc can migrate and “once deposited onto epithelial cells, it can cause chronic inflammation, leading to a series of mutagenic events, and this effect is worse in talc contaminated with asbestos, a known carcinogen.”<sup>30</sup> Further, since 2020, the Environmental Protection Agency (EPA) has twice noted that asbestos can be in talc and that it is a human carcinogen.<sup>31</sup> Related to these scientific events is the recent decision in July 2024 by the International Agency for Research on Cancer (IARC) to reclassify talc as a 2A (probable carcinogen) based in part on the “*strong mechanistic evidence* that talc exhibits key characteristics of carcinogens, including inducing chronic inflammation and altering cell proliferation, cell death, or nutrient supply.”<sup>32</sup> This is further support for Judge Wolfson’s holdings on pages 173 and 177 of the *Daubert* Opinion.

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<sup>27</sup> *Id.* (citing O’Brien (2020)).

<sup>28</sup> NIH/NIEHS Environment Factor, Ex. 1.

<sup>29</sup> *Daubert* Opinion at 168-172

<sup>30</sup> Kemi Ogunsina, et al., *Association between Genital Talc and Douche Use in Early Adolescence or Adulthood with Uterine Fibroid Diagnosis*, 229 Am. J. Obst. & Gyn. 665 (2023), attached as **Exhibit 9**.

<sup>31</sup> 89 Fed. Reg. 21970 (May 28, 2024) (to be codified at 40 C.F.R. pt. 751), attached as **Exhibit 10**.

<sup>32</sup> Stayner (2024), Ex. 2.

- **Dose Response:** With respect to dose response factors considered by Judge Wolfson, there is additional cohort evidence that further strengthens support for this factor. As the NIH Study authors noted in their 2024 article, evidence from cohort data demonstrated that the risk increased from 1.81 to 2.01 in women who used genital talc more frequently and for longer durations.<sup>33</sup> This finding was confirmed by NIH which summarized that evidence and stated the “strongest associations observed for frequent and long-term users and use during reproductive years.”<sup>34</sup> Further a pooled cohort study found a 1.4 increased risk for daily users in an analysis of Nurse’s Health Study cohort data and an overall risk of between 31% and 65% for frequent use across all combined studies.<sup>35</sup>

In addition to the post-2020 epidemiologic studies, the work of authoritative national and international scientific organizations further supports a causal effect.

First, Health Canada issued its final assessment of talc and ovarian cancer in 2021, considering the arguments of Defendants and Defendants’ experts, and concluded that genital talc causes epithelial ovarian cancer.

Second, the International Agency for Research on Cancer (IARC), an agency of the World Health Organization, recently upgraded its carcinogenic categorization of talc without asbestos to a probable ovarian carcinogen (Group

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<sup>33</sup> O’Brien (2024), Ex. 8, at 13.

<sup>34</sup> NIH /NIEHS Environmental Factor, Ex. 1; *see also* ASCO Press Release, attached as **Exhibit 11**.

<sup>35</sup> Sean A. Woolen, et al., *Association between the Frequent Use of Perineal Talcum Powder Products and Ovarian Cancer: A Systematic review and Meta-Analysis*, 37 J. Gen. Intern. Med. 2526 (2022), attached as **Exhibit 12**.

2A) and reaffirmed its 2012 assessment that talc with asbestos is an ovarian carcinogen (Group 1).

Third, the NIH has affirmed this year that there is “compelling evidence” that genital talc use is associated with an increased risk of ovarian cancer.

Fourth, the Environmental Protection Agency (EPA) has concluded that talc with asbestos causes ovarian cancer.

**A. Strength of Association: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That Genital Talc Use Is Associated With An Increased Risk of Ovarian Cancer**

Judge Wolfson correctly noted that the “strength of association” factor considers the relative risk, *i.e.*, the “ratio of the incidence rate of disease in exposed individuals to the incidence rate in unexposed individuals.”<sup>36</sup> Defendants’ pre-2020 scientific argument against this “strength of association” factor was simple and mechanical: while case control epidemiologic studies and meta-analyses of epidemiologic studies did show that genital talc was associated with a 1.2-1.6 increased risk, the prospective cohort studies did not. Defendants argued that case-control studies were allegedly lower on the evidentially “hierarchy” than cohort studies and suggested that the case control studies were effectively cancelled out.<sup>37</sup>

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<sup>36</sup> *Daubert* Opinion at 162 (citation omitted).

<sup>37</sup> *Daubert* Opinion, 509 F Supp at 164-5 (“Defendants submit that there is a hierarchy of observational epidemiologic studies, which include[s] in descending order of reliability — cohort studies, case control studies and cross-sectional

As extensively briefed before Judge Wolfson, J&J's 2020 analysis of the "hierarchy of evidence" was wrong. There is no sound scientific basis upon which to argue that a whole body of science is effectively "cancelled" because of an immutable pecking order of scientific design, particularly where the cohort studies were not designed to study the talc ovarian cancer question and were underpowered to do so.<sup>38</sup>

But there is no need to revisit J&J's debate about the so-called "hierarchy." Now, in 2024, there are at least three published, peer-reviewed papers from cohort studies or reporting data from a cohort study which were not available to Judge Wolfson in 2020—O'Brien (2020), O'Brien (2024), and Woolen (2022)—that show a statistically significant increased risk of epithelial ovarian cancer with genital talc use, particularly with frequent use.

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studies."). In addition to the scientific argument, J&J made a legal argument that a "1.2 to 1.6 relative risk identified by the experts is a "weak, not strong association by any objective measure." 509 F. Supp at 163 and n. 26 (citing *Carl v. Johnson & Johnson*, Nos. ATL-L-6540-14, 2016 N.J. Super. Unpub. LEXIS 2102, 2016 WL 4580145 at \*18 (N.J. Super. Ct. Law Div. Sept 2, 2016). The *Carl* case was overruled on appeal. *Carl v. Johnson & Johnson*, 464 N.J. Super. 446 (App. Div. 2020). Other than the trial court in *Carl* (since reversed), not a single court has found that the epidemiologic evidence as relied on by Plaintiffs' experts is unreliable.

<sup>38</sup> Kenneth J. Rothman, *Six Persistent Research Misconceptions*, 29 J. Gen. Intern. Med. 1060, 1060 (2014), attached as **Exhibit 13** ("[M]indlessly ascribing a greater validity to a study based on a hierarchy of study designs is fallacious.").

## 1. O'Brien (2020)

The first Cohort Study that was not available for Judge Wolfson's consideration in 2020 is O'Brien (2020), a study of pooled cohort studies authored by NIH scientists. O'Brien (2020) shows a positive association between genital talc use and ovarian cancer, with a statistically significant risk in women with intact reproductive system.

Before discussing O'Brien (2020), however, it is important to note the cohort data Judge Wolfson reviewed in 2020. As she noted, there were three individual prospective cohort studies prior to 2020 that studied the relationship between genital talc use and ovarian cancer. These three individual prospective cohort studies did not show a statistically significant positive association for epithelial ovarian cancer generally. As Plaintiffs' experts explained at the time, however, these three individual cohort studies had significant limitations because, among other things, they were "underpowered" to detect a result, collected limited and incomplete data about talcum powder use, and none was specifically designed to study the talc and ovarian cancer question.<sup>39</sup> Moreover, Plaintiff's experts testified that there were biases in these cohort studies that would attenuate or mask a true association. Under those circumstances, Judge Wolfson agreed that Plaintiffs' experts' "decision to rely on case-control studies, as opposed to the three

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<sup>39</sup> See *Daubert* Opinion, 509 F Supp. at 166.

cohort studies, is supported by good grounds and does not constitute a ‘rigid’ dismissal of the cohort studies.”<sup>40</sup>

O’Brien (2020) attempted to address the shortcomings of the three pre-2020 cohort studies. Significantly, those shortcomings are the same shortcomings that Plaintiffs’ experts testified about at the *Daubert* hearing (and that defense experts denied). According to the NIH scientists in O’Brien (2020):

3 large cohort studies have assessed the association between use of powder in the genital area and ovarian cancer risk, with inconsistent results. However, ovarian cancer is a rare disease (1.3% lifetime risk in the United States), and individual cohort studies are not sufficiently powered to detect modest associations, particularly if restricted to susceptible subgroups, such as women with patent reproductive tracts (*i.e.*, having an intact uterus and no tubal ligation).<sup>41</sup>

Because of the limitations posed by the individual cohort studies, the NIH authors pooled the results of all the cohort studies together with the goal of increasing their ability to detect modest results.

While the pooled O’Brien (2020) study sought to determine the overall risk—including women with closed reproductive tracts (*i.e.*, women who had hysterectomies or a tubal ligation) and those with open reproductive (*i.e.*, patent) tracts—the particular interest was in women who had intact reproductive tracts. The reason for the interest in the “patent tube” subgroup was “because patency is

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<sup>40</sup> *Id.*

<sup>41</sup> *See* O’Brien (2020) at 50.



required for there to be a direct pathway between the application area and the ovaries . . .”<sup>42</sup> When the analysis was done, the researchers found an increased overall risk of 1.08 (CI 0.99-1.17), *i.e.*, an 8% increased risk. Notably, they also found a statistically significant increased risk in women with intact reproductive tracts of 13%, *i.e.*, 1.13 (1.01-1.26).<sup>43</sup>

In prior pleadings, Defendants called the statistically significant increased risk in women with intact reproductive systems “one weak finding” which, in their view, contradicts the overall result of “no association.”<sup>44</sup> In the recent expert depositions, Defendants’ experts have reiterated that interpretation, *i.e.*, that there is no positive association.

Defendants’ tortured interpretation of O’Brien (2020), however, is at odds with how the NIH researchers themselves have described their findings. Contrary to Defendants’ experts’ opinions, **the NIH researchers noted that their study showed a *positive* association between genital talc use and ovarian cancer of which the statistically significant results in women with patent tubes was a critical part.** For example, in response to a Letter to the Editor by Harlow and Rothman, the NIH authors directly addressed questions raised concerning their

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<sup>42</sup> *Id.* at 51. This is but one place where the NIH authors noted the biological plausibility of talc with or without asbestos causing ovarian cancer.

<sup>43</sup> *Id.* at 53-4.

<sup>44</sup> See, e.g., Opposition to Motion to Reconsider (ECF No. 32026) at 11-12.

findings and clarified that their overall findings were positive and likely underestimated the true risk of association:

***If cohort studies (pooled HR, 1.08) are likely biased toward the null and case-control studies (meta-analysis OR, 1.35) are likely biased away from the null, the true association may lie somewhere in the middle.***

We completely agree with Dr Harlow and colleagues that our results, particularly the analyses limited to women with intact reproductive tracts, should not be discounted because of lack of statistical significance . . . ***we never equated the lack of statistical significance to evidence of no association.***<sup>45</sup>

With respect to the findings in women with patent reproductive tracts, the NIH authors further explained that these were important findings that should not be ignored but that supported an association between talc and ovarian cancer:

We conducted subgroup analyses with an a priori hypothesis that intact reproductive tracts are required to be susceptible to the exposure. Therefore, even though we stated that findings from subgroup analyses should be interpreted as exploratory, we do not consider them all equally important and ***agree that the positive association among women with patent reproductive tracts (HR, 1.13; 95%CI, 1.01-1.26) is consistent with the hypothesis that there is an association between genital powder use and ovarian cancer.***<sup>46</sup>

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<sup>45</sup> *Id.* (emphasis added).

<sup>46</sup> *Id.* To deflect from the NIH's actual statements, J&J is likely to suggest that the response was prompted by a letter written by Harlow and Rothman, who subsequently became experts for the Plaintiffs. While Dr. Rothman has been withdrawn as an expert, he was not a Plaintiffs' expert at the time the letter was written and was, in fact, was previously a consultant for Defendants. See Expert Report of Drs. Rothman and Harlow, attached as **Exhibit 14**. Importantly, Judge Wolfson relied on Dr. Rothman, 509 F. Supp at 172, and his textbooks on epidemiology are cited as authoritative by the Reference Manual on Scientific Evidence. At the time these letters were written, Dr. Harlow, who has published

In numerous articles published since 2020, NIH authors have restated over-and-over again that the results of O'Brien (2020) should **not** be read as evidence of no association. Instead, they have emphasized that the results showed a positive association that was likely understated, particularly among women with intact genital tracts. Indeed, the NIH authors used O'Brien (2020) in support of a positive association between genital talc use and ovarian cancer in the cohort studies, not the lack of an association as J&J and its experts would have the reader believe. For example, NIH authors cited their 2020 study for the following propositions:

- “The epidemiologic literature **supports** a possible positive association between genital talc use and ovarian cancer”<sup>47</sup>
- “In the largest prospective study so far, the OC3 found a very small **positive** association between genital powder use and ovarian cancer risk among all women (Hazard Ratio HR 1.08 [(CI 0.99-1.17] as well as among women with intact uterus and fallopian tubes (HR 1.13) (CI 1.01-1.26)].”<sup>48</sup>
- “The HR from a pooled analysis of prospective cohort studies also indicated **a positive**, albeit small association (HR 1.08), and as previously noted, this effect estimate is likely biased toward the null because of nondifferential misclassification of exposure.”<sup>49</sup>

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several studies on talc and ovarian cancer going back to 1989, was not a Plaintiffs' expert. What is important is the NIH authors agree with the comments raised by Drs. Harlow and Rothman.

<sup>47</sup> Katie O'Brien, et al., *The Association between Douching, Genital Talc Use, and the Risk of Prevalent and Incident Cervical Cancer*, 11 Nature 14836, 2 (2021) (emphasis added), attached as **Exhibit 15**.

<sup>48</sup> Mary K. Townsend, et al., *Cohort Profile: The Ovarian Cancer Cohort Consortium (OC3)*, 51 Int'l J. Epidemiology 73, 94(2022), attached as **Exhibit 16**.

<sup>49</sup> O'Brien (2024), Ex. 8, at 13.

- [Since 2006] more consistent *positive associations have been reported in pooled cohort studies* and case control studies...”<sup>50</sup>

This additional evidence from O’Brien (2020) supports a positive association seen in the case control studies and the meta-analyses. This study further supports Judge Wolfson’s 2020 *Daubert* opinion.

## 2. O’Brien (2024)

The second relevant study that was not available to Judge Wolfson at the time of her *Daubert* ruling is O’Brien (2024). This study was published by the same NIH scientists who published O’Brien (2020). O’Brien (2024) data and the analysis were derived from the Sister Study, a large cohort study. O’Brien (2024) “supports a positive association between genital talc use and ovarian cancer consistent with previous studies.”<sup>51</sup> The NIH chose to feature O’Brien (2024) to highlight its importance and, in so doing, noted that it “**provides compelling evidence that genital talc use is associated with an increased risk of ovarian**

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<sup>50</sup> Stayner (2024), Ex. 2, at 2 (citing O’Brien (2020)).

<sup>51</sup> *Id.* at 13. J&J designated a new expert, John Kornak, Ph.D., to attack O’Brien (2024). He opines that O’Brien (2024) was “flawed” and should never have passed peer-review. The PSC has contemporaneously filed a *Daubert* Motion to exclude his opinions. Attached to that Motion as an Exhibit is the rebuttal Expert Report of Elizabeth Stuart, Ph.D., Professor and Chair in the Department of Biostatistics at Johns Hopkins Bloomberg School of Public Health. As detailed in her report, Dr. Stuart opines that the peer-reviewed methods for O’Brien (2024) are best practices in the statistical community.

**cancer” with the “strongest assertions observed for frequent use and long term use during the reproductive years.”<sup>52</sup>**

As a preliminary matter, the same NIH authors published a 2016 study from the same cohort—one of the cohort studies that Defendants and their experts relied heavily upon before Judge Wolfson.<sup>53</sup> Gonzales (2016) studied women who used genital talc only “recently” (or at ages 10-13) and who had been followed for only 6.6 years. Predictably, Gonzales (2016) showed no association between “recent” talc use and ovarian cancer. In O’Brien (2024), the authors addressed the significant and obvious limitations of Gonzales (2016), namely, the short follow-up period which, for O’Brien (2024) was now 13 years and, most significantly, new data and information on lifetime talc use obtained through a follow-up questionnaire that the study authors did not have for the Gonzales (2016).

When the additional follow up time and information on lifetime talc use was considered, the NIH authors found a statistically significant increased risk of 1.82 (CI 1.36-2.43), which became even more pronounced with long term talc use. The NIH authors further noted that the study was consistent with the positive results found in their pooled study, O’Brien (2020). According to the NIH authors:

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<sup>52</sup> NIH/NIEHS Environmental Factor, Ex. 1

<sup>53</sup> Gonzales, et al., *Douching, Talc and Risk Of Ovarian Cancer*, 27 Epidemiology 797 (2016), attached as **Exhibit 17**.

Using newly collected data on intimate care product use in a large cohort of US women, we found evidence supporting a positive association between ever genital talc use and incident ovarian cancer.<sup>54</sup>

The additional evidence from O'Brien (2024) further supports the positive association seen in the case control studies and the meta-analyses. In other words, it lends support to the strength of association between genital talc and ovarian cancer. If this evidence had been available at the time of the *Daubert* hearing, Judge Wolfson would most certainly have determined that the evidence further supported the association she found, which was a relative increased risk of ovarian cancer between 1.2-1.6.

### **3. Woolen (2022)**

The third peer-reviewed study containing cohort data that was not available in 2020 is Woolen (2022).<sup>55</sup> Woolen (2022) was designed to estimate whether there is an association between frequent use of genital talc and ovarian cancer. Woolen (2022) looked at both case control and cohort study data that reported talc use of equal to or more than two times a week. Among other things, the Woolen (2022) authors looked at daily use data from the Nurses Health Cohort Study, to determine whether frequent exposure was related to ovarian cancer.

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<sup>54</sup> *Id.* at 13 (emphasis added).

<sup>55</sup> Woolen (2022), Ex. 13.

In Woolen (2022), the authors found “frequent use of perineal talcum powder was associated with an increased risk of ovarian cancer, with a pooled adjusted odds ratio of 1.47. (CI 1.31-1.65).”<sup>56</sup> When the authors looked solely at the Nurse’s Health Study cohort data the odds ratio was 1.40 (CI 1.31, 1.65).

This collection of peer reviewed studies, O’Brien (2020), O’Brien (2024), and Woolen (2022), provide additional cohort study data on strength of association that Judge Wolfson didn’t have available in 2020. Collectively, these studies now add to the already strong body of literature and further confirm the strength of association ranging from an odds ratio of 1.2-1.6 based on data from both prospective and retrospective studies, with a higher risk of association for long term and frequent users of talcum powder.

**B. Consistency of Association: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence of “Consistency” Between Studies Of Genital Talc Use And Ovarian Cancer**

As Judge Wolfson noted, “[t]he Consistency factor considers whether the results of the relied on studies have been replicated.”<sup>57</sup> In 2020, Defendants’ argument against consistency centered on a claim that is not much different than its claim about the strength of association:

Defendants contend that the epidemiological studies are not, in fact, consistent, in that the cohort and case-control studies have reached

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<sup>56</sup> See Woolen (2022) at 2530.

<sup>57</sup> *Daubert* Opinion, 509 F. Supp at 168.

different results. (*See* Defs.' Post-Hr'g Br., at 19.) In other words, Defendants argued that because no cohort study concluded there was a statistically significant association between talc use and ovarian cancer, the two types of studies cannot be consistent. (*See id.*; *see also* Defs.' General Causation Reply Br., at 26.)<sup>58</sup>

Putting aside the significant methodological question of whether a positive but not statistically significant result is “inconsistent” with a positive statistically significant one - an issue that the Court already resolved,<sup>59</sup> there is consistency

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<sup>58</sup> *Id.*

<sup>59</sup> The role of statistical significance was the subject of significant briefing before Judge Wolfson. Epidemiologists are taught that “significance testing” is poor practice. As Judge Wolfson noted, the textbook *Modern Epidemiology*, which is relied on as authoritative in the Judicial Manual for Scientific Evidence, makes the following point:

Dr. Kenneth Rothman, a leading epidemiologist, in *Modern Epidemiology*... opined that “[i]t is sometimes claimed that a literature or set of results is inconsistent simply because some of the results are statistically significant and some are not. This sort of evaluation is completely fallacious even if one accepts the use of significance testing methods.” (*Id.* at 934-35.) In other words, according to the experts, in the epidemiology context, inconsistent statistical significance from one study to the next does not, in of itself, show inconsistency under Bradford Hill.

While Defendants may disagree with the general causation expert's approach to statistical significance, the Court does not find that their methodology is unreliable and unsupported by science. Rather, at this stage, I find that they have provided detailed reasons for their findings and their approach to considering statistical significance within the studies in determining consistency.

*Daubert* Opinion at 169; *see also Retire Statistical Significance: More than 800 Signatories Call For and End of Hyped Claims and Dismissal of Possibly Crucial Effects*, 657 Nature 305 (2019), attached as **Exhibit 18** (“Neither should we



between the case control studies and the cohort studies based on the new cohort data. Even using Defendants' experts' disfavored "significance testing" method—that both case control and cohort studies must show a statistically significant increased risk—they do. As the NIH Sisters Study investigators observed in O'Brien (2024):

***Our findings of a positive association between genital talc use and ovarian cancer are consistent with previous studies.*** Pooled analyses or meta-analyses of case-control studies have produced odds ratios of 1.2-1.4. The HR from a pooled analysis of prospective cohort studies also indicated a positive, albeit small association (HR 1.08), and as previously noted, this effect estimate is likely biased toward the null because of nondifferential misclassification of exposure.<sup>60</sup>

The IARC Working Group that examined talc just this month made the same point about the consistencies between case control and cohort studies:

Since [2006] more ***consistent positive associations*** for ever-use versus never-use ***have been reported in pooled cohort studies and case control studies***, including evidence of the exposure-response relationship with frequency or duration of use.<sup>61</sup>

The evidence of consistency across study designs of all types is greater now than it was when Judge Wolfson considered the *Daubert* Opinion.

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conclude that two studies conflict because one had a statistically significant result and the other did not") and *Six Persistent Research Misconceptions*, Ex. 13 ("Significance testing has led to far more misunderstanding and misinterpretation than clarity in interpreting study results").

<sup>60</sup> *Id.* at 13 (citations omitted).

<sup>61</sup> Stayner (2024), Ex. 2.

**C. Biologic Plausibility: Post-2020 Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence Supporting Plaintiffs’ Claim That It Is Biologically Plausible That Talc Causes Ovarian Cancer**

As Judge Wolfson noted, the Bradford Hill consideration of “biologic plausibility” considers whether “the purported association [is] biologically plausible and consistent with existing scientific knowledge.”<sup>62</sup> As was pointed out in the *Daubert* Opinion, “plausibility” does not equal “proof”:

Biological plausibility does not require certainty or even proof for the biological mechanism in question—the relevant question is “whether the hypothesized causal link is credible in light of what is known from science and medicine about the human body and the potentially offending agent.”<sup>63</sup>

Rather than being undermined, since 2020, the plausibility of talcum powder (and whatever contaminants are contained in it) migrating through the genital tract and causing inflammation and oxidative stress has been specifically acknowledged in the scientific literature. A couple of examples in the post-2020 peer-reviewed literature that strengthen Judge Wolfson’s conclusion for “biologic plausibility” between genital talc and ovarian cancer are:

- By irritating epithelial ovarian tissue or fallopian tubes directly, powder could induce an inflammatory response even in the absence of asbestos. This could set off a cascade of increased

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<sup>62</sup> *Daubert* Opinion, 509 F Supp 3d at 172.

<sup>63</sup> *Id.* at 174 (citing *Milward v. Acuity Specialty Prods. Grp., Inc.*, 639 F.3d 11, 25 (1st Cir. 2011)).

oxidative stress levels, DNA damage, and cell division, all of which could contribute to carcinogenesis.<sup>64</sup>

- Talc applied to underwear, sanitary napkins, diaphragms, or directly to the perineal region can enter the vagina and travel up the reproductive tract. Talc particles may act as irritants, inciting an inflammatory response... Additional or more severe adverse effects could occur if the talc contained asbestos, a known carcinogen sometimes mined in the same locations as talc. The epidemiologic literature supports a possible positive association between genital talc use and ovarian cancer...<sup>65</sup>
- Another example of an inflammatory factor involved in the carcinogenesis of OvCa is the use of talcum powder in the genital area. Talc, along with associated components such as asbestos or quartz, which are known carcinogens and can contaminate talc products, might ascend through the genital tract and irritate the epithelial lining of the fallopian tubes or ovaries. This could possibly trigger an inflammatory response that may promote carcinogenesis. Taken together, epidemiological data suggest that there may be a small positive association between the use of genital powder and OvCa.<sup>66</sup>
- Talc is a poorly soluble particle, and animal models have shown that once deposited onto epithelial cells, it can cause chronic inflammation, leading to a series of mutagenic events, and this effect is worse in talc contaminated with asbestos, a known carcinogen. Some douching products contain phthalates, which are endocrine-disrupting chemicals (EDCs) that can be detrimental to human health.<sup>67</sup>

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<sup>64</sup> O'Brien (2020) at 56. (citations omitted).

<sup>65</sup> O'Brien (2021) at 2 (citations omitted).

<sup>66</sup> Manuel Sanchez-Prieto, et al., *Etiopathogenesis of Ovarian Cancer: An Inflammaging Entity?*, 42 Gyn. Onc. Reports 101018 at 3 (2022) (citations omitted), attached as **Exhibit 19**.

<sup>67</sup> Ogunsina (2023), Ex. 9, at 1 (citations omitted); *see also* Minh Tung Phung, et al., *Effects of Risk Factors for Ovarian cancer in Women with and without Endometriosis*, 118 Fertility and Sterility 960, 965 (2022), attached as **Exhibit 20**. Not only do the authors call talc use a "well established risk factor" for ovarian

Far from undermining Judge Wolfson’s 2020 discussion on “biologic plausibility,” post-2020 literature provides additional support that the talc-ovarian cancer association is plausible. As described in the post-2020 literature, the biological evidence supports the view that the consistent association seen in the epidemiologic studies—both case control and cohort studies—is causal.

**D. Dose Response: Post-2020 Cohort Study Evidence Further Supports Judge Wolfson’s 2020 Finding That There Is Evidence Supporting A Dose Response Between Genital Talc Use And Ovarian Cancer**

As Judge Wolfson correctly noted, evidence of a dose response provides “strong, but not essential” evidence that the relationship between agent and disease is causal.”<sup>68</sup> Judge Wolfson found that “based on epidemiologic principles, a strong dose response is not necessarily required to find a casual nexus.”<sup>69</sup> Nevertheless, Judge Wolfson noted that there was evidence of dose-response between genital talc use and ovarian cancer, particularly with respect to a pooled study of case-control studies from Terry, et al.<sup>70</sup> and the meta-analysis by

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cancer, they note that the inflammation mechanism is plausible, stating: ***“inflammation has been proposed as a possible biologic mechanism for talc’s association with ovarian cancer.”***; see also O’Brien (2021) (“When powder is applied to the genital areas, it has the potential to reach internal reproductive organs and promote carcinogenesis by irritating and inflaming exposed tissues.”).

<sup>68</sup> *Daubert* Opinion, 509 F. Supp. 3d at 177.

<sup>69</sup> *Id.* at 179.

<sup>70</sup> Kathryn L. Terry, et al., *Genital Powder Use and Risk of Ovarian Cancer: A Pooled Analysis of 8,525 Cases and 9,859 Controls*, 6 Cancer Prevention Research 811 (2013), attached as **Exhibit 21**.

Penninkilampi.<sup>71</sup> Since 2020, there has been additional evidence—primarily from cohort studies—that show a dose response. Specifically, both O’Brien (2024) and Woolen (2022) showed a dose response.

In O’Brien (2024), the NIH scientists noted an increased risk in frequent users (81%) and long-term users (101%) as compared to sometimes users (18%) and short-term users (17%), with the former results being statistically significant.<sup>72</sup>

As noted in that study:

The association between genital talc use and ovarian cancer was higher for frequent (recall bias corrected-HR [HRrb], 1.81 [95% CI, 1.29 to 2.53]) and long-term users (HRrb, 2.01 [95% CI, 1.39 to 2.91]), compared with never users (both P for trend 5 .001; ) Genital talc use during a woman’s 20s and 30s was positively associated with incident ovarian cancer, but HRs were near null for teen use.<sup>73</sup>

In its report on the study, the NIH scientists made clear that “the strongest associations were observed for frequent and long-term users and for use during reproductive years.”<sup>74</sup>

The consistency of findings on the frequency issue and dose response evidence raised by Judge Wolfson is further confirmed by the findings in O’Brien (2024) and Woolen (2022). In Woolen (2022), the authors looked at both cohort

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<sup>71</sup> Ross Penninkilampi, et al., *Perineal Talc Use and Ovarian Cancer: A Systematic Review and Meta-Analysis*, 29 *Epidemiology* 41, 41 (2018), attached as **Exhibit 22**.

<sup>72</sup> O’Brien (2024) at 10, Table 3.

<sup>73</sup> O’Brien (2024) at 13.

<sup>74</sup> *Id.*

and case control studies that reported frequent talc use, at least twice a week.<sup>75</sup>

The authors found that “frequent use of perineal talcum powder is associated with an increased risk of ovarian cancer, with a pooled adjusted odds ratio of 1.47 (95% CI 1.31, 1.65).”<sup>76</sup> Similarly, there is ample evidence of dose response beyond that which Judge Wolfson considered in 2020.

**E. Actions By Authoritative National And International Scientific Bodies After Judge Wolfson’s 2020 *Daubert* Opinion Further Support A Causal Effect**

In 2020, Judge Wolfson noted that, at that time, there did not appear to be a “consensus” on the issue of talc and ovarian cancer. Since the 2020 *Daubert* Opinion, respected scientific bodies have looked at the causal relationship between talc and ovarian cancer. The actions of these bodies have further supported a causal effect. These authorities include Health Canada, IARC, the NIH, and the EPA.

**1. Health Canada**

In her opinion, Judge Wolfson noted the Bradford Hill analysis contained in the Draft Health Assessment performed by Health Canada, the Canadian regulatory equivalent to the FDA.<sup>77</sup> In 2021, following the issuance of the Court’s *Daubert*

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<sup>75</sup> Woolen (2022) at 2526.

<sup>76</sup> *Id.* at 2530.

<sup>77</sup> *See Daubert* Opinion, 509 F. Supp at 185 & n 49.

Opinion, Health Canada issued its Final Health Assessment.<sup>78</sup> As set forth above, that final assessment considered both the input of Defendants and the input of Defendants’ general causation experts, including Drs. Merlo and Diette. It applied a full Bradford Hill analysis which “under[went] external peer review.”<sup>79</sup> After an exhaustive analysis, Health Canada concluded that:

With regards to perineal exposure, analyses of the available human studies in the peer reviewed literature indicate a consistent and statistically significant positive association between perineal exposure to talc and ovarian cancer. *The available data are indicative of a causal effect.* Given that there is potential for perineal exposure to talc from the use of certain self-care products (e.g., body powder, baby powder, diaper and rash creams, genital antiperspirants and deodorants, body wipes, bath bombs, bubble bath), a potential concern for human health has been identified.<sup>80</sup>

## 2. The International Agency for Research on Cancer (IARC)

In 2020, Judge Wolfson noted that IARC had classified Talc as a “possible” ovarian carcinogen in 2006. That changed in 2024. Looking at the totality of the scientific evidence, IARC upgraded talc without asbestos from “possibly carcinogenic” (Group 2B) to “**probably carcinogenic**” (Group 2A) with respect to ovarian cancer (emphasis added).<sup>81</sup> Important to the issues in this case, IARC reaffirmed its 2012 classification that talc *with asbestos* is, without question, an

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<sup>78</sup> Health Canada Health Assessment, Ex. 4.

<sup>79</sup> *Id.* at 2

<sup>80</sup> *Id.* at iii.

<sup>81</sup> Stayner (2024), Ex. 2.

ovarian carcinogen (Group 1) and noted that “[t]alc products with asbestos has been documented and [i]ndustry standards used to assess talc in cosmetic and pharmaceutical *products have not been sufficiently sensitive to rule out contamination with asbestos.*”<sup>82</sup>

### 3. The Environmental Protection Agency

In 2023, the EPA issued a final rule under the Toxic Substances Control Act (TSCA), related to reporting and recordkeeping requirements under the TSCA. In this final rule, the EPA concluded as follows: (1) asbestos may occur as an impurity in talc; (2) talc deposits can contain asbestos as an impurity; and (3) asbestos can cause ovarian cancer.<sup>83</sup> A year later, in 2024, the EPA again addressed the issue with a final rule related to the use of chrysotile asbestos. In this rule, the EPA stated as follows: (1) talc deposits and articles that contain talc have been shown to contain asbestos; and (2) chrysotile asbestos can cause ovarian cancer.<sup>84</sup>

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<sup>82</sup> Stayner (2024), Ex. 2; IARC, Ex. 3.

<sup>83</sup> 88 Fed. Reg. 47782, 47790 (July 25, 2023) (to be codified at 40 C.F.R. pt. 704).

<sup>84</sup> 89 Fed. Reg. 21970, 21970 & 21973.



#### 4. National Institutes of Health

In its feature of O'Brien (2024), the NIH noted that there is now “compelling evidence” that genital talc use is associated with an increased risk of ovarian cancer, particularly among “long term users.”<sup>85</sup>

#### CONCLUSION

For the above stated reasons, and in response to the Court's April 30, 2024 Order, the PSC states that Chief Judge Wolfson's 2020 *Daubert* Opinion adheres to Rule 702, even as clarified by the 2023 amendments; and (2) the “new” science and literature published since 2020 not only supports Chief Judge Wolfson's previous findings but also demonstrates that the *Daubert* Opinion regarding general causation was correct.

Dated: July 23, 2024

Respectfully submitted,

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<sup>85</sup> NIH/NIEHS Environmental Factor, Ex. 1.

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